Table 1

SYSTEM CONFIGURATION

SYSTEM (symbol in Fig. 7)	MEMBRANE ANNEALING	MEMBRANE THICKNESS (mil)
1 (*)	NO	2.0
2 ( )	YES	3.0
3 (■)	NO	3.5
4 (Δ)	YES	2.0
5 (▲)	NO	2.0

[00069] A backing member comprised of a multilaminate of polyester thylene, aluminum, polyester and EVA (Scotchpak 1220, 3M Co., St. Paul, MN) was also provided and the aqueous gel was pouched between the backing member and the release liner/adhesive/rate controlling membrane on a rotary heat-seal machine. Sealed pouches in sizes of 5 cm^2 were die cut and immediately pouched to avoid loss of ethanol. The pouched systems were allowed to equilibrate for at least two weeks in order to reach equilibrium concentration of the drug and ethanol in the rate controlling and adhesive layers.

[00070] The peelable liner of the laminate was removed and the fentanyl releasing surface was placed against the stratum corneum side of a disc of human epidermis which had been blotted dry just prior to use. The excess epidermis was wrapped around the device so that none of the device edge was exposed to the receptor solution. The device covered with epidermis was then mounted on a Teflon® holder of a release rate rod using nylon mesh and metal string. The rod was then reciprocated in a fixed volume of receptor solution (0.05M phosphate buffer, pH 6.5) at 35°C.

[00071] At given time intervals, the entire receptor solution was removed from the test tubes and replaced with an equal volume of fresh receptor solutions previously equilibrated at 35°C. The receptor solutions were stored in capped vials at 4°C until assayed for fentanyl base or ethanol content by HPLC analysis. From the drug concentration and the volume of the receptor

solutions, the area of permeation and the time interval, the flux of the drug was calculated as follows: (drug concentration X volume of receptor)/(area x time) = flux ($\mu g/cm^2$ hr).

[00072] Figure 7 depicts the *in vitro* flux of fentanyl through skin from the systems prepared as set forth above. As seen in Figure 7, the systems comprising the annealed rate controlling membranes demonstrated a higher flux of fentanyl therethrough as compared to the non-annealed systems. There was significantly less variation of drug fluxes between the systems comprising the annealed membranes as compared to the variation in fluxes observed among the systems comprising non-annealed membranes.

[00073] Figure 8 depicts the *in vitro* flux of ethanol through skin from the systems prepared as set forth above. As seen in Figure 8, the systems comprising the annealed rate controlling membranes demonstrated a more consistent, higher flux of ethanol therethrough as compared to the systems with non-annealed membranes.

EXAMPLE 2

[00074] Systems comprising 2 mil, 3 mil, or 3.5 mil EVA (9% VA) membranes and a surface area of 10 cm^2 were prepared according to the procedure set forth in Example 1. The 2.0 mil EVA membranes in roll form were annealed in a sauna room at 60°C for 2-34 hours, while the 3.0 and 3.5 mil EVA membranes were annealed in an oven at 60°C for two hours. The release rates of fentanyl and ethanol from systems comprising annealed membranes were then measured and compared to release rates measured from control systems comprising non-annealed membranes.

[00075] Release rates were measured by placing the systems in closed jars containing a fixed amount of a receptor solution (0.05M phosphate buffer, pH 6.5) at 35°C. At given time intervals, the entire receptor solution was removed from the jars and replaced with an equal volume of fresh

receptor solutions previously equilibrated at 35°C. The receptor solutions were stored in capped vials at 4°C until assayed for fentanyl base or ethanol content by HPLC analysis. From the drug concentration and the volume of the receptor solutions, the area of permeation and the time interval, the flux of the drug was calculated as follows: (drug concentration X volume of receptor)/(area x time) = flux ($\mu g/cm^2$ hr). The average *in vitro* release rate of fentanyl and ethanol are shown in Table 2.